IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Dean L. Engelhardt et al..

Serial No. 08/486,069 Group Art Unit: 1631

Filed: June 7, 1995 Examiner: Ardin Marschel, Ph.D.

Title: NUCLEIC ACID SEQUENCING PROCESSES USING MODIFIED NUCLEOTIDES OR NUCLEOTIDE ANALOGS, AND OTHER PROCESSES FOR NUCLEIC ACID DETECTION AND CHROMOSOMAL CHARACTERIZATION USING SUCH MODIFIED NUCLEOTIDES OR NUCLEOTIDE ANALOGS (As Amended)

TRANSMITTAL
SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

HON. COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Sir:

Transmitted herewith is a Supplemental Information Disclosure Statement which is being filed in accordance with 37 C.F.R.§§1.56 and 1.97-1.98. The items listed on Form PTO-1449, a copy of which is enclosed, may be deemed to be pertinent to the above-identified application and are made of record to assist the Patent and Trademark Office in its examination of this application. The Examiner is respectfully requested to fully consider the items and to independently ascertain their teaching.

1. [ ] For each of the following items listed on the enclosed copy of Form PTO-1449 that is not in the English language, an English language translation of that item or a portion thereof or a concise explanation of the relevance of that item is enclosed:

2. [ ] For each of the following items listed on the enclosed copy of form PTO-1449 that is not in the English language, a concise explanation of the relevance of that item is incorporated in the specification of the above-identified application.

EXPRESS MAIL CERTIFICATE
"Express Mail" Label No.: EL531126132US Deposit Date: May 23, 2000 I hereby certify that this paper and the attachments herein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.110 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 Ronald C. Fedus Reg. Exhibit 32,567 — MAY 23 2000 Date

Enz-5(D8)(C2)

3. [ ] Any copy of the items on the enclosed copy of Form PTO-1449 that is not enclosed with this Information Disclosure Statement was previously cited by or submitted to the Patent and Trademark Office in the prior [ ] Divisional or [ ] Continuation-In-Part application under 37 C.F.R. §1.60, U.S. Serial No. _____, filed _____.

4. [ ] No fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with:

   [ ] 37 C.F.R. §1.97(b)(1), within three months of the filing date of the above-identified application.

   [ ] 37 C.F.R. §1.97(b)(2), within three months of the date of entry into the national stage as set forth in §1.491 in an international application.

   [ ] 37 C.F.R. §1.97(b)(3), before the mailing date of a first Office action on the merits.

5. [ ] No fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a Notice of Allowance (where there has been no prior final action), and is accompanied by one of the certifications pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below.

6. [x] A fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a notice of allowance (where there has been no prior final action):

   [ ] A check in the amount of $240.00 is enclosed in payment of the fee.

   [x] Charge the fee to Deposit Account No. 05-1135, Order No. ENZ-5(D8)(C2). A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

7. [ ] A fee is due under 37 C.F.R. §1.17(i)(1) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(d), after the mailing date of a final action or a notice of allowance, whichever comes first, but before payment of the issue fee, and is accompanied by:

   a. one of the certification pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below; and

   b. the attached petition requesting consideration of this Information Disclosure Statement; and

   c. the fee due under 37 C.F.R. §1.17(i)(1) which is paid as set forth in paragraph 10 below.

8. [ ] A fee is due under 37 C.F.R. §1.17(i)(1) for this Information Disclosure Statement since it is being filed in compliance with:

   a. [ ] 37 C.F.R. §1.313(b)(3), after the issue fee has been paid and information cited in this Information Disclosure Statement may render at least one claim unpatentable and is accompanied by the attached Petition To Withdraw Application From Issue;

3. [ ] Any copy of the items on the enclosed copy of Form PTO-1449 that is not enclosed with this Information Disclosure Statement was previously cited by or submitted to the Patent and Trademark Office in the prior [ ] Divisional or [ ] Continuation-In-Part application under 37 C.F.R. §1.60, U.S. Serial No. _____, filed _____.

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   [ ] 37 C.F.R. §1.97(b)(1), within three months of the filing date of the above-identified application.

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   [ ] 37 C.F.R. §1.97(b)(3), before the mailing date of a first Office action on the merits.

5. [ ] No fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a Notice of Allowance (where there has been no prior final action), and is accompanied by one of the certifications pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below.

6. [x] A fee is due under 37 C.F.R. §1.17(p) for this Information Disclosure Statement since it is being filed in compliance with 37 C.F.R. §1.97(c), after the period specified in paragraph 4 above but before the mailing date of a final action or a notice of allowance (where there has been no prior final action):

   [ ] A check in the amount of $240.00 is enclosed in payment of the fee.

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   a. one of the certification pursuant to 37 C.F.R. §1.97(e) set forth in paragraph 9 below; and

   b. the attached petition requesting consideration of this Information Disclosure Statement; and

   c. the fee due under 37 C.F.R. §1.17(i)(1) which is paid as set forth in paragraph 10 below.

8. [ ] A fee is due under 37 C.F.R. §1.17(i)(1) for this Information Disclosure Statement since it is being filed in compliance with:

   a. [ ] 37 C.F.R. §1.313(b)(3), after the issue fee has been paid and information cited in this Information Disclosure Statement may render at least one claim unpatentable and is accompanied by the attached Petition To Withdraw Application From Issue;

b. [ ] 37 C.F.R. §1.313(b)(5), after the issue fe has been paid and information cited in this Information Disclosure Statement is to be considered in a Continuation application upon abandonment of the instant application and is accompanied by the attached Petition To Withdraw Application From Issue.

c. [ ] The fee due under 37 C.F.R. §1.17(i)(1) is paid as set forth in paragraph 10 below.

9. [ ] I hereby certify that each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.

[ ] I hereby certify that no item of information in the Information Disclosure Statement filed herewith was cited in a communication from a foreign patent office in a counterpart foreign application or, to my knowledge after making reasonable inquiry, was known to any individual designated in ∋1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

10. [ ] A check in the amount of $130.00 is enclosed in payment of the fee due under 37 C.F.R. §1.17(i)(1).

[ ] Charge the fee under 37 C.F.R. ∋1.17(i)(1) to Deposit Account No. 05-1135. Order No. _____. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

[x] The Commissioner is hereby authorized to charge any additional fees which may be required for this Information Disclosure Statement, or credit any overpayment to Deposit Account No. 05-1135. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

Dated: May 23, 2000

By: _____
RONALD C. FEDUS
Registration No. 32,567

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Dean L. Engelhardt et al.	
Serial No.	08/486,069	Group Art Unit: 1631
Filed:	June 7, 1995	Examiner: Ardin Marschel, Ph.D.
Title:	NUCLEIC ACID SEQUENCING PROCESSES USING MODIFIED NUCLEOTIDES OR NUCLEOTIDE ANALOGS, AND OTHER PROCESSES FOR NUCLEIC ACID DETECTION AND CHROMOSOMAL CHARACTERIZATION USING SUCH MODIFIED NUCLEOTIDES OR NUCLEOTIDE ANALOGS (As Amended)	

527 Madison Avenue, 9th Floor
New York, New York 10022
May 23, 2000

FILED VIA EXPRESS MAIL

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §§1.56 & 1.97-1.98

Dear Sirs:

Pursuant to the provisions of 37 C.F.R. §§1.97-1.98, and in full compliance with their duty of disclosure under 37 C.F.R. §1.56, Applicants, through their attorney, are bringing the following sixty-eight (68) documents to the attention of the U.S. Patent and Trademark Office and the Examiner handling their above-identified application:

EXPRESS MAIL CERTIFICATE

"Express Mail" Label No.: EL531126132US
Deposit Date: May 23, 2000

I hereby certify that this paper and the attachments herein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.110 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231

Ronald C. Fedus
Reg. Exhibit 32,567

MAY 23 2000
Date

Enz-5(D8)(C2)

1. Scheit, Karl H., Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, Inc., New York, New York 1980, 288 pages [Exhibit 1];

2. Kornberg, A., DNA Synthesis, W. H. Freeman And Company, San Francisco, 1974, Chapter 7, pages 227-228 [Exhibit 2];

3. Kornberg, A., DNA Replication, W. H. Freeman And Company, San Francisco, 1980, Chapter 12, "Inhibitors of Replication," pages 415-441 [Exhibit 3];

4. Adams, R. L. P. et al., Davidson's The Biochemistry of the Nucleic Acids, 8th Edition, Academic Press, New York, 1976, Chapter 11 "Replication of DNA," pages 298-299 [Exhibit 4];

5. Langen, P., Antimetabolites of Nucleic Acid Metabolism: The Biochemical Basis of Their Action, with Special Reference to their Application in Cancer Therapy, Gordon and Breach, New York, English edition translated from the German by Dr. Thomas A. Scott, 1975, pages 143-187 [Exhibit 5];

6. Darlix et al., "Analysis of Transcription *in Vitro* Using Purine Nucleotide Analogs," Biochemistry 10:1525-1531 (1971) [Exhibit 6];

7. Geider, K., "DNA Synthesis in Nucleotide-Permeable *Escherichia coli* Cells: The Effects of Nucleotide Analogues on DNA Synthesis," European Journal of Biochemistry 27:554-563 (1972) [Exhibit 7];

8. Darlix and Fromageot, "Restriction of gene transcription by nucleotide analogs," Biochimie 56:703-710 (1974) [Exhibit 8];

9. Marcus, F., "Inhibition of Fructose 1,6-Biphosphatase by 9-ß-D-Arabinofuranosyl 5'-Monophosphate," Cancer Research 36:1847 (1976) [Exhibit 9];

10. Simoncsits and Tomasz, "A New Type of Nucleoside 5'-Triphosphate Analogue: P1-(Nucleoside 5'-) P1-Amino-Triphosphates," Tetrahedron Letters 44:3995-3998 (1976) [Exhibit 10];

11. Chladek et al., "Synthesis and Properties of Nucleoside 5'-Phosphoazidates Derived from Guanosine and Adenosine Nucleotides: Effect on Elongation Factors G and Tu Dependent Reactions," Biochemistry 16:4312-4319 (1977) [Exhibit 11];

12. Piperno and Alberts, "An ATP Stimulation of T4 DNA Polymerase Mediated via T4 Gene 44/62 and 45 Proteins," Journal of Biological Chemistry 253:5174-5179 (1978) [Exhibit 12]

13. Reha-Krantz et al., "Bacteriophage T4 DNA Polymerase Mutations That Confer Sensitivity to the PPi Analog Phosphonoacetic Acid," Journal of Virology 67:60-66 (1993) [Exhibit 13];

14. Birch and Lee, "Structural Functions and Taste in the Sugar Series: The Structural Basis of Bitterness in Sugar Analogues," Journal of Food Science 41:1403-1407 (1976) [Exhibit 14];

15. Lartey and Derechin, "Preparation and Study of a Fluorescent Sugar Analog: Competitiv Inhibitor of Yeast Hexokinase," Preparative Biochemistry 9:85-95 (1979) [Exhibit 15];

16. Roberts and Hayes, "Effects of 2-deoxy D-glucose and other sugar analogues on acid production from sugars by human dental plaque bacteria," Scandinavian Journal of Dental Research 88:801-809 (1980) [Exhibit 16];

17. Kortnyk et al., "CMP and CMP-sugar analogs as inhibitors of sialic acid incorporation and glycoconjugates," Eur. J. Med. Chem. - Chimica Therapeutica 15:77-84 (1980) [Exhibit 17];

18. Keppler et al., "Uridylate trapping, induction of UTP deficiency, and stimulation of pyrimidine synthesis *de novo* by D-galactosone," Biochemical Journal 206:139-146 (1982) [Exhibit 18];

19. Yang and Metzler, "Pyridoxal 5'-Phosphate and Analogs as Probes of Coenzyme-Protein Interaction," Methods in Enzymology 62:528-551 (1979) [Exhibit 19];

20. Stridh et al., "The Effect of Pyrophosphate Analogues on Influenza Virus RNA Polymerase and Influenza Virus Multiplication," Archives of Virology 61:245-250 (1979) [Exhibit 20];

21. Stoeckler et al., "Human Erythrocyte Purine Nucleoside Phosphorylase Reaction with Sugar-Modified Nucleoside Substrates," Biochemistry 19:102-107 (1980) [Exhibit 21];

22. Ryser et al., U.S. Patent No. 4,847,240 [Exhibit 22];

23. Schwartz et al., U.S. Patent No. 5,212,059 [Exhibit 23];

24. Banker et al., U.S. Patent No. 5,643,730 [Exhibit 24];

25. Usman et al., U.S. Patent No. 5,652,094 [Exhibit 25];

26. Eigén et al., U.S. Patent No. 5,807,677 [Exhibit 26];

27. Liu et al., U.S. Patent No. 5,914,230 [Exhibit 27];

28. Wright et al., U.S. Patent No. 5,998,383 [Exhibit 28];

29. Pagano et al., U.S. Patent No. 5,242,906 [Exhibit 29];

30. Ecker et al., U.S. Patent No. 5,591,600 [Exhibit 30];

31. Anderson et al., U.S. Patent No. 5,591,720 [Exhibit 31];

32. Cook et al., U.S. Patent No. 5,614,617 [Exhibit 32];

33. Baker, U.S. Patent No. 5,643,780 [Exhibit 33];

34. Rahman et al., U.S. Patent No. 5,665,710 [Exhibit 34];

35. Ecker et al., U.S. Patent No. 5,736,294 [Exhibit 35];

36. Crooke et al. , U.S. Patent No. 5,811,232 [Exhibit 36];

37. Ecker et al., U.S. Patent No. 5,874,564 [Exhibit 37];

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39. Montgomery, J. H. and H. Jeanette Thomas, "4-Amino-7-β-D-Ribofuranosyl-7H-Imidazol[4,5-*d*]-v-Triazine(2-Aza-Adenosine) The Synthesis of 2-Azapurine Nucleosides from Purine Nucleosides Accomplished via Ring Opening Followed by Reclosure with Nitrous Acid," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 118, pages 681-685 [Exhibit 39];

40. Shibaev, V. N. and S. M. Spiridonova, "1-Methyladenosine-5'-(α- -Glucopyranosyl Pyrophosphate): Methylation of Adenosine Derivatives," in Synthetic Procedures in Nucleic Acid Chemistry, Volume I, Werner Zorbach and R. Stuart Tipson, Editors, Interscience Publishers, New York, 1968, No. 14, pages 461-462 [Exhibit 40];

41. Thomas, H. Jeanette and J. A. Montgomery, "3-Benzylpurines," in Synthetic Procedures in Nucleic Acid Chemistry, Volume I, Werner Zorbach and R. Stuart Tipson, Editors, Interscience Publishers, New York, 1968, No. 10, pages 28-30 [Exhibit 41];

42. Yamamoto et al., "Adenine-N-oxide produced from adenine with gamma-rays and its binding to SH protein," J. Radiation Research 21:239-247 (1980) [Exhibit 42];

43. Rhaese, H. J., "Chemical Analysis of DNA Alterations: III. Isolation and Characterization of Adenine Oxidation Products Obtained from Oligo- and Monodeoxyadenylic Acids Treated with Hydroxyl Reactions," Biochimica et Biophysica Acta 166:31-326 (1968) [Exhibit 43];

44. Taylor, M. R., "Metal Binding to Nucleic Acid Constituents. The Crystal Structure of Trichloroadeniniumzinc(III)," Acta Crystallogr. B29:884-890 (1973) [Exhibit 44];

45. Walker et al., "The Interaction of H+, Zn2+, and Cu2+ With Adenine and Guanine," Australian Journal of Chemistry 26:2391-2399 (1973) [Exhibit 45];

46. Srinivasan et al., "X-Ray Crystal Structure of Zinc-Adenine and Zinc-Guanine Complexes," J. Chemical Society D24:1668-1669 (1970) [Exhibit 46];

47. Kaneko et al., "8,2-Anhydrides of Purine -8-Thiol Nucleosides (or of Purine 2'-Thionucleosides): Synthesis of 8,2'-Anhydronucleosides of Purine-8-thiol [or of 8,2'-Anhydro-(2'-thionucleosides)] by use of Diphenyl Carbonate as the Cyclizing Agent," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 103, pages 395-399 [Exhibit 47];

48. Robins, M. J. and G. L. Bason, "6-Chloro-9-(2-Deoxy-β-D-Erythro-Pentofuranosyl)Purine from the Chlorination of 2'-Deoxyinosine: Direct Replacement of the 6-Oxo Group by a Chlorine Atom in a Purine 2'-Deoxynucleoside: Stabilization of the Glycosyl Bond Towards Cleavage by Acid," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 104, pages 601-606 [Exhibit 48];

49. Zemlicka, J. and J. Owens, "6-Chloro-9-β-D-Ribofuranosylpurine: A Versatile Intermediate in the Synthesis of Purine Ribonucleosides," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 106, pages 611-614 [Exhibit 49];

50. Kochetkov et al., "3-Methyluridine 5'-Phosphate: Methylation of Uridine Derivatives with Diazomethane: Phosphorylation of Nucleosides with Pyrophosphonyl Chloride," in Synthetic Procedures in Nucleic Acid Chemistry, Volume I, Werner Zorbach and R. Stuart Tipson, Editors, Interscience Publishers, New York, 1968, No. 152, pages 497-499 [Exhibit 50];

51. Zemlicka, J., "3-Methyl-6-Azauridine [4-Methyl-2-β-D-Ribofuranosyl-AS-Triazin-3,5-(2H,4H)-Dione]: Alkylation of a Nucleoside Antimetabolite by Use of N,N-Dimethyl-formamide Dimethyl Acetal," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 78, pages 451-453 [Exhibit 51];

52. Piskala, A. and F. Sorm, "1-β-D-Ribofuranosyl-δ-Triazine-2,4-(1H,3H)-Dione (5-Azauridine): Direct Synthesis of a 5-Azauridine Ribonucleoside by the Fisher-Helferich Procedure," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 79, pages 455-459 [Exhibit 52];

53. Poverenny et al., "Immunological Approaches to DNA Structure Investigation - I: Immunological Identification of the Product of Cytosine Modification with Bisulfite and *O*-Methylhydroxylamine Mixture," Molecular Immunology 16:313-316 (1979) [Exhibit 53];

54. Visser, D. W. and P. Roy-Burman, "5-Hydroxyuridine 5-Phosphate Derivatives: Substitution Reactions at the Pyrimidine Ring of Nucleotides," in Synthetic Procedures in Nucleic Acid Chemistry, Volume I, Werner Zorbach and R. Stuart Tipson, Editors, Interscience Publishers, New York, 1968, No. 151, pages 493-496 [Exhibit 54];

55. Cadet, J., "1-(2-Deoxy--β-D-Erythro-Pentopyranosyl)Uracil and Its α-D Anomer: Acid-Catalyzed Isomerization of the Glycosyl Group in 5,5-Dibromo-2'-deoxy-5,6-dihydro-6-hydroxyuridine," Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Part Two, Dr. Leroy B. Townsend and Dr. R. Stuart Tipson, Editors, John Wiley & Sons, New York, 1978, No. 55, pages 311-315 [Exhibit 55];

56. Kondo et al., "Functional Monomers and Polymers, 77[a]: On the Synthesis and Polymerization of Acryloylamino Derivatives of Nucleic Acid Bases," Makromol. Chem., Rapid Commun. 1:303-306 (1980) [Exhibit 56];

57. Nair et al., "Utility of Purinyl Radicals in the Synthesis of Base-Modified Nucleosides and Alkylpurines: 6-Amino Group Replacement by H, Cl, Br, and I," Journal of Organic Chemistry 45:3969-3974 (1980) [Exhibit 57];

58. Fujii et al., "Purines. XXI.1) Synthesis of Adenine 1-Oxides Carrying an Allylic Side Chain at the 9-Position," Chem. Pharm. Bull. 28:3443-3446 (1980) [Exhibit 58];

59. Hiraoka, K. and T. Yokoyama, "Syntheses and characterization of polymers containing nucleic acid bases," Int. J. Biolog. Macromolecules 1:50-54 (1979) [Exhibit 59];

60. Zeleznick, L. D., "6-Amino-9-(4-Dimethylaminobutyl)-9*H*-Purine," in Nucleic Acid Chemistry: Improved and New Synthetic Procedures, Methods and Techniques, Drs. Leroy B. Townsend and R. Stuart Tipson, Editors, John Wiley & Sons, Inc., 1978, pages 17-18 [Exhibit 60];

61. Watson, A. A., "Purine *N*-Oxides. LVII. 9-Hydroxyhypoxanthine, Xanthine, and Guanine," Journal of Organic Chemistry 39:2911-2916 (1974) [Exhibit 61];

62. Helfer et al., "Selective Alkylation and Aralkylation of Cytosine at the 1-Position," Journal of Organic Chemistry 46:4803-4804 (1981) [Exhibit 62];

63. Hosmane, R. S. and N. J. Leonard, "Simple Convenient Synthesis of 1-Methylcytosine," Synthesis 2:118-119 (1981) [Exhibit 63];

64. Hayashi et al., "*N*-Alkylation of Cytosine and Its Nucleosides with Trialkyl Phosphates," Bull. Chem. Soc. Japan 53:277-278 (1980) [Exhibit 64];

65. Kondo et al., "Synthesis of Sulfonic Acid Derivatives of Purine and Pyrimidine," Synthetic Communications 10:267-271 (1980) [Exhibit 65];

66. Pitha, J. and P. O. P. Ts'o, "N-Vinyl Derivatives of Substituted Pyrimidines and Purines," Journal of Organic Chemistry 33:1341-1344 (1968) [Exhibit 66];

67. Inaki et al., "Synthesis of Poly-L-Lysine Containing Nucleic Acid Bases," in Modification of Polymers, Charles E. Carraher, Jr. and Minoru Tsuda, Editors, ACS Symposium Series 121, American Chemical Society, Washington, D.C., 1980, pages 359-370 [Exhibit 67]; and

68. Shimidzu et al., "Synthesis of Cationic Mononucleotide Analogs and Their Interaction with Polynucleotide and Polynucleotide Analogs," Bulletin of the Chemical Society of Japan 52:3362-3365 (1979) [Exhibit 68].

The above-submitted documents [Exhibits 1-68] were cited by applicants in previous responses. Karl H. Scheit's book, Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, Inc., New York, 1980, Exhibit 1 above, was discussed briefly at the May 8, 2000 interview with the Examiner. A completed Form PTO-1449 listing the sixty-eight (68) above-submitted documents is also attached hereto as Exhibit 69.

By this voluntary citation of art, Applicants and their attorney are requesting that the documents be made of record in the instant application.

The above citation of references is not a representation that thes documents constitut a complete or exhaustiv listing, nor that the above listing n cessarily

includes the closest or most relevant references, nor are these documents necessarily a complete listing of all references known to Applicants or their attorney. It is simply a voluntary citation of references made in good faith, which is not intended to serve in any way as a substitute for the Examiner's own search.

In view of the general and specific features described and claimed in the present application, Applicants respectfully submit that the present invention is neither suggested nor disclosed by the documents referred to above and is thus patentably distinct thereover.

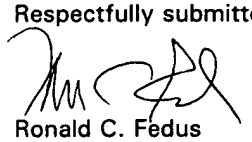
Applicants do not believe, and do not submit, by the citation of these references, that these references, either by themselves or in combination with other references, render the invention prima facie obvious under the new duty of disclosure rules.

Applicants respectfully request that the Examiner make the above-submitted documents of record in the instant application. Applicants further request that the Examiner consider these documents as any of them may relate to the instant application.

The fee under 37 C.F.R. §1.17(p) for filing this Information Disclosure Statement is $240.00. The Patent and Trademark Office is hereby authorized to charge the amount of this fee (and any other fees in connection with this IDS) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

Respectfully submitted,

MAY 23, 2000



Ronald C. Fedus
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Attorney for Applicants

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Form PTO-1449 U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office INFORMATION DISCLOSURE CITATION (use several sheets if necessary)	Atty. Docket No. ENZ-5(D8)(C2)	Serial No. 08/486,069
	Applicants: Dean L. Engelhardt et. al.	
	Filed: June 7,. 1995	Group: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPRO-PRIATE
		4 8 4 7 2 4 0		Ryser			
		5 2 1 2 0 5 9		Schwartz			
		5 6 4 3 7 3 0		Banker			
		5 6 5 2 0 9 4		Usman			
		5 8 0 7 6 7 7		Eigen			
		5 9 1 4 2 3 0		Liu			
		5 9 9 8 3 8 3		Wright			
		5 2 4 2 9 0 6		Pagano			
		5 5 9 1 6 0 0		Ecker			
		5 5 9 1 7 2 0		Anderson			
		5 6 1 4 6 1 7		Cook			
		5 6 4 3 7 8 0		Baker			

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		5 7 3 6 2 9 4		Ecker			
		5 8 1 1 2 3 2		Crooke			
		5 8 7 4 5 6 4		Ecker			
		5 8 9 1 4 6 8		Martin			

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